تێبینی: هەچ هەڵەیەکی تێدابوو، خۆت ڕاستیبکەرەوە.

Glycosides

Define?

Two parts: 1- aglycone part, 2- glycone part.

Two types of sugar: 1- normal (D-glucose), 2- abnormal (glucuronic acid; used by liver).

Two enzymes hydrolyze a number of glycoside: 1- emulsin (almond kernels), 2- myrosinase (black mustard seeds).

Classification of glycosides according to:

1) **Pharmacological:** e.g. cardiotonic glycoside. (ignore chemical structure).
2) **Sugar part:** (ignore chemical property and pharmacological activity).
3) **Glycone part:** (give information about chemical nature and pharmacological activity).

Chemical nature of the "aglycone" part: "name + glycoside"

1- Anthraquinone	**4- Flavonol**	**7- Phenolic**
2- Saponin	**5- Alcohol**	**8- Glucosinolate**
3- Cynogenic	**6- Aldehyde**	**9- Steroidal**

1- Anthraquinone (contain anthracene) (Str.)

Use: cathartic (increase tone of smooth muscle of colon, secretion of water and electrolyte into large intestine, evacuation of large bowel).

Causes of constipation:

1) **Drug induces:** e.g. **Verapamil** (hypertension).
2) **Tannins:** e.g. tea.
3) **Disease induced:** e.g. 1- heart failure, 2- IBS (irritable bowel syndrome), 3- colon cancer.

Used in **small dose**.

Long term causes: laxative dependence and loss of normal bowel movement.

High dose causes:

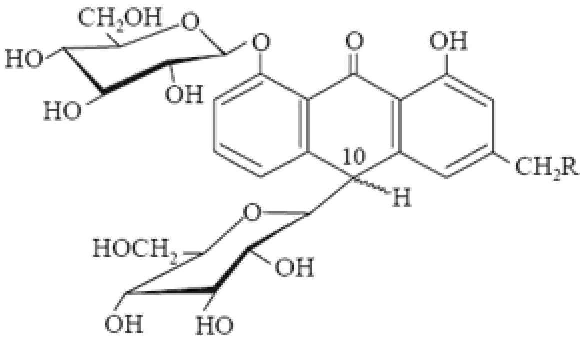
1) Slow down of colon. 2) The tone of colon will be lost.

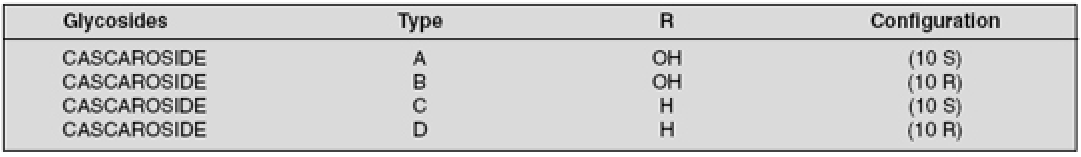
1- Cascara sagrada
2- Frangula
3- Rhubarb
4- Aloe
5- Senna

1) **Cascara sagrada: (Str.)**
   Plant name**: Rhamnus purshianus**
   Fam.: **Rhamnaceae**
   Plant part: **Bark**

Should be used after one year? Because this glycoside are converted to monomeric oxidized glycoside which exhibit a milder cathartic activity. (**with structure**)

Four types of "cascaroside" "A, B, C, D"





Glycosides	Type	R	Configuration
CASCAROSIDE	A	OH	(10 S)
CASCAROSIDE	B	OH	(10 R)
CASCAROSIDE	C	H	(10 S)
CASCAROSIDE	D	H	(10 R)

Side effects:

1) Loss of normal tone of bowel.
2) Lose ability to absorb Ca^{+2} and Fe^{+2}, excreted, so it is not used of lactated women, pregnancy, children and old age cause **bone deformation**, **osteoporosis**, **anemia**.
3) Anti-viral, anti-cancer, anti-bacterial activity. (inhibit glycosylation and glycoprotein formation, so kill the virus).

2) **Frangula or (Buckthorn bark)**
   Plant name: **Rhamnus frangula**
   Fam.: **Rhamnaceae**

Have activity of cascara, **not used?** (cause: **gripping**, **spasm**).

3) **Rhubarb**
   Plant name: **Rheum officinale**
   Fam.: **Polygonaceae**

4) **Aloe (Str. P. 54)**
   Plant Name: **Aloe barbadensis**
   Common type: **Aloe vera**
   Fam.: **Liliaceae**

Have **cathartic activity**.

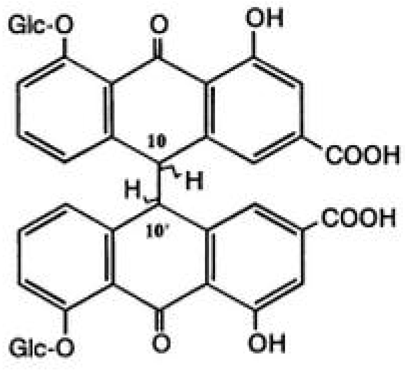
Double bond stabilized, has anti-oxidant activity.

Contain (**Salicylate, prostaglandin, mineral**):

1) Anti-inflammatory
2) Wound healing
3) Anti-viral
4) Anti-bacterial
5) Enhance fibroblast formation

5) **Senna (str.)**
   Senna acutifolia (leaves) (sharply pointed leaflet)
   Senna angustifolia (narrow leaved)
   Fam.: **Fabaceae**

Senna	Cascara
cheap	Expensive
Less side effect	More side effect
Less gripping action	More gripping action
The **leave** used	The **root** used



ئەم ڕەسمە خۆت بیکێشە وەك ئەوەی دکتۆر.
دوو گلوکۆزەکەی بکێشە.
لەگەڵ دوو (H)ەکەش، ئەوەی سەرەوە لە دواوەیە
و ئەوەی خوارەوەش لە پێشەوە.

2- Saponin glycoside

Name? Because when shaken with water form spot, surface active agent. Or (mixed with water form colloidal).

Glycyrrhizin (Str. P. 56)
Glycyrrhiza glabra
Fam.: **Leguminosae**
Plant part: **root**
Treatment: **peptic ulcer**

Dried rhizoms used for extraction.
It is 50 times sweeter than sugar, **used as:** 1- sweetening agent, 2- for making taste of drug better (quinine-anti malarial).

Uses:

1) decreases acid secretion.
2) Increase secretion from globular cell inverted within the columnar cell lining the stomach, (**treatment:** 1- peptic ulcer, 2- duodenal ulcer).

3- Cyanogenic glycoside

By hydrolysis form (HCN + toxic).
HCN interfere mitochondria respiratory chain, leading to **1- hypoxia, 2- cyanosis, 3- brain damage, 4- coma, 5-death**.
Used by **plant** as: **1- antibacterial, 2- antifungal**.
Plants contain cyanogenic glycoside (**bitter almond, apricot, peach**).

Amygdalin
Prunus amygdalus
Prunus serotina
Fam.: **Rosaceae**

Cyanogenic glycoside **uses**: **1- flavoring agent, 2-** for controlling **sickle cell anemia**, **3-** anti-cancer agent.
Biosynyhesis pathway: (important!)

4- Alcohol glycoside (Str.)

Salix fragilis salicin & salicyl alcohol structure?
Salix purpurea
Fam.: **Salicaceae**

Inflammation reaction:

$$\textbf{Arachidonic acid} \xrightarrow[\textbf{Cyclo-oxygenase}]{\textbf{cox}} \textbf{peroxide} \longrightarrow \textbf{PGS (prostaglandin)}$$

Anti-inflammatory drug (**NSATD, steroidal drug**).
The drug is not specific, block synthesis of all types of PGS, thus decrease proliferation of mucous membrane and decrease secretion of mucous form globlet cells inverted within the epithelia of the stomach and finally causing gastric ulcer.
1- flat structure, 2- carboxylic acid which is ionized in body, 3- ionized part soluble in gastric fluid, 4-contain lipophilic part it helps to penetrate mucous membrane.

Aspirin (acetyl salicylic acid):
Low dose < 100 mg **anticoagulant**
< 300 mg **analgesic**
< 500 mg **anti-inflammatory (Rheumatic fever) (block Cox-1 cyclo-oxygenase)**
Salicylic acid control pain and inflammation by two mechanisms:

1) Direct contact with mucosa of gastric.
2) Inhibition of both processes of prostaglandin synthesis.

5- Aldehyde glycoside

Vanilin (Str.)
Vanilia tahitensis
Fam.: **Orchidaceae**
Use: **flavoring agent**

6- Isothiocyanate glycoside

Mustard
Fam.: **Brassicaceae**

Black mustard	White mustard
Brassica nigra	Brassica alba
Contain **sinigrin** which is an **aliphatic**	Contain **sinalbin** which is **aromatic**
More odor	Less odor
Allyl	**Aryl**

Sinalbin (C-S-C): an e.g. for C-S-C glycosidic linkage.
Uses:

1) Anti-cancer agent (estrogen-linked mammary carcinoma).
2) Expectorant (congestion of nose).

7- Hydroquinone glycoside

Disease: **hyperpigmentation** (accumulation of melanin-dark spot).
Hydroquinone: inhibition of melanin formation, repair skin that has dark spot.

8- Steroidal glycoside

Defined as those type of glycosides that upon hydrolysis yield steroidal nucleus called (**cyclopentanoperhydrophenanthrene**).
Cis-fusion: has a good pharmacological activity.

Digitais glycoside
Use: heart failure, some arrhythmia
Common name: **Foxglove**
A- Digitalis lanata
B- Digitalis purpurea
Fam.: **Scrophulariaceae**

Digitoxin: Major part of action is **lactone ring**. If lost by metabolism, pharmacological action lost. Hydration of double bond leads to less pharmacological activity.

Digoxin: obtained from dried leave of digitalis lonata.

Opening of the lactone ring render the drug inactive.

Some reductases break the double bond and decrease activity.

Digoxin has more water solubility because of the presence of more hydroxyl group, form hydrogen bond with water, so has short half-life and excreted.

But **digitoxin** has one hydroxyl group on carbon no. 12 that cause not to solubilize in water and not easily excreted by kidney and conc. Increase reach toxic level, and excreted mostly by bile and also by kidney. Secondary problem to heart failure.

Toxic level in very close to therapeutic level so monitoring should be used directly, at toxic level may directly kill the patient.

Specific antibody mask the effect of **digitoxin**.

myocardium:

1- Have the ability to conduct electrical impulses, when there is changes in the environmental interstitial, change in Ca, Na when excited one cell excite another.
2- Self-conduction by itself, have ability to contract by itself, without stimulation by another system.

Atrial fibrillation is serious, not fatal.

Ventrical arrhythmia, directly cause death.

Arrythmia: irregularity in the contraction of myocardium.

Mechanism:

1) Activate vagus nerve, decrease heart rate.
2) Improve myocardial contraction by inhibition the system Na/K-ATPase (cardiotonic; increase tone of contraction).
3) Antiarrhythmic; by prolongation of depolarization of myocardial cell.

digoxin	**digitoxin**
More water soluble (more hydroxyl group)	Less water soluble (less hydroxyl group)
Eliminated by kidney	Eliminated mostly by bile
Therapeutic level: 0.2 ng/mL	Therapeutic level: 16-24 ng/mL
Toxic level: 2.5 ng/mL	Toxic level: 37 ng/mL

Diuretic drugs reduce fluid levels in the body by increasing fluid excretion; because diuretics are often prescribed for patients with heart failure who may also be taking digoxin, **if digoxin given without diuretic drug, fluid accumulates in the glomerulus**. Diuretics reduce fluid retention and may cause low potassium, so potassium supplement should be given to supplement potassium lost by diuretic drugs.

Also called **cardenolide**.

Apocynaceae: used for poison of plant to form digitoxin.